(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 024 587**
A1

(12) EUROPEAN PATENT APPLICATION

(21) Application number: 80104623.6

(22) Date of filing: 06.08.80

(51) Int. Cl.³: C 07 C 87/28
C 07 C 87/45, C 07 C 93/14
C 07 D 211/14, C 07 D 307/81
C 07 D 333/58, A 61 K 31/13
A 61 K 31/34, A 61 K 31/38
A 61 K 31/445

(30) Priority: 22.08.79 CH 7656/79

(43) Date of publication of application:
11.03.81 Bulletin 81/10

(84) Designated Contracting States:
AT BE CH DE FR GB IT LI LU NL SE

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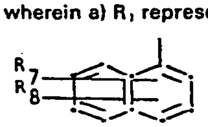
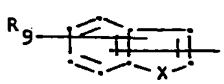
(54) Propenylamines, processes for their production, pharmaceutical compositions containing them and their use as pharmaceuticals.

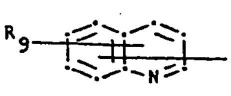
(57) Compounds of formula I

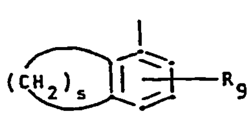
$$R_2-\overset{R_1}{\underset{R_3}{C}}-\overset{R_4}{N}-\overset{R_5}{CH}-CH=CH-R_6 \qquad I$$

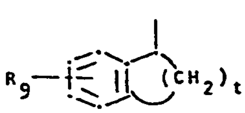
wherein a) R_1 represents a group of formula

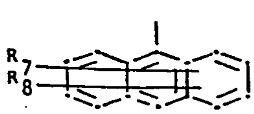

IIa


IIb


IIc


IId


IIe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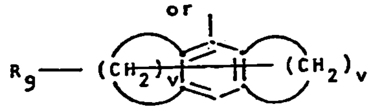
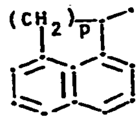
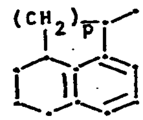
 IIg

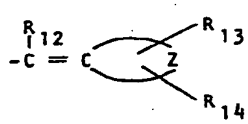
and R_2 represents hydrogen or lower alkyl, or R_1 and R_2 together represent a group of formula

 IIh  IIi

whereby in the formulae IIa to IIi,
R_7 and R_8 represent, independently, hydrogen, halogen, trifluoromethyl, hydroxy, nitro, lower alkyl or lower alkoxy,
R_9 represents hydrogen, halogen, hydroxy, lower alkyl or lower alkoxy,
X represents oxygen, sulphur, imino, lower alkyl imino or a radical of formula $-(CH_2)_r-$,
p is 1, 2 or 3,
r is 1, 2 or 3,
s is 3, 4 or 5,
t is 2, 3 or 4, and
v is 3, 4, 5 or 6;
R_3 and R_5 represent, independently, hydrogen or lower alkyl, and
R_4 represents C_{1-6} alkyl or C_{3-8} cycloalkyl-(C_{1-6})-alkyl; and
R_6 represents a group of formula

$-C \equiv C-R_{11}$ IIIa $\quad -\underset{R_{11}}{\underset{|}{C}} = CH_2$ IIIb

oder

 IIIc

wherein R_{11} represents hydrogen, optionally α-hydroxy substituted alkyl; alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, phenyl, phenalkyl or thienyl,
R_{12}, R_{13} and R_{14} represent, independently, hydrogen or lower alkyl, and $=\overset{\frown}{C\;\;Z}$ represents a C_{3-8} cycloalkylidene radical optionally containing a double bond; or
b) R_1 represents a group of formula IIa to IIg as defined under a),
R_2 represents hydrogen or lower alkyl,
R_3 and R_4 together form a group $-(CH_2)_u-$,
wherein u is an integer of 1 to 8, and
R_5 and R_6 have the meanings given under a).
processes for their production, their use as pharmaceuticals and pharmaceutical compositions containing them.

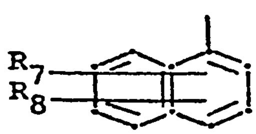
PROPENYLAMINES, PROCESSES FOR THEIR PRODUCTION, PHARMACEUTICAL COMPOSITIONS CONTAINING THEM AND THEIR USE AS PHARMACEUTICALS

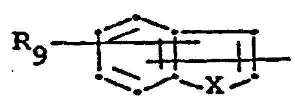
This invention relates to propenylamines, processes for their production, pharmaceutical compositions containing them and their use as pharmaceuticals.

The invention provides compounds of formula I,

$$R_2 - \underset{\displaystyle R_3}{\overset{\displaystyle R_1}{C}} - \overset{\displaystyle R_4}{N} - \overset{\displaystyle R_5}{CH} - CH = CH - R_6 \qquad \text{I}$$

wherein a) R_1 represents a group of formula


IIa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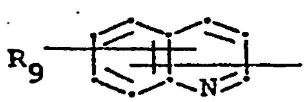
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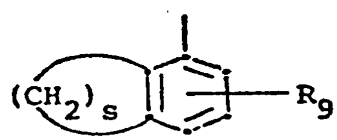
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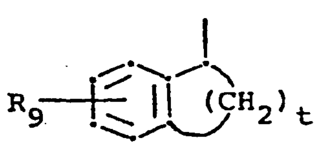
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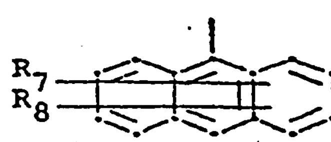
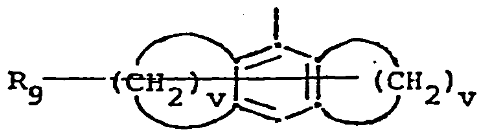
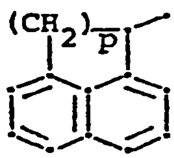

IIf

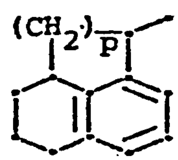
or

 IIg

and R_2 represents hydrogen or lower alkyl,

or R_1 and R_2 together represent a group of formula

 IIh

 IIi

whereby in the formulae IIa to IIi,

R_7 and R_8 represent, independently, hydrogen, halogen, trifluoromethyl, hydroxy, nitro, lower alkyl or lower alkoxy,

R_9 represents hydrogen, halogen, hydroxy, lower alkyl or lower alkoxy,

X represents oxygen, sulphur, imino, lower alkyl imino or a radical of formula $-(CH_2)_r-$,

p is 1, 2 or 3,

r is 1, 2 or 3,

s is 3, 4 or 5,

t is 2, 3 or 4, and

v is 3, 4, 5 or 6;

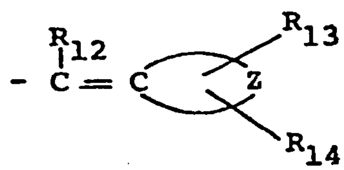
R_3 and R_5 represent, independently, hydrogen or lower alkyl, and

R_4 represents C_{1-6}alkyl or C_{3-8} cycloalkyl-(C_{1-6})-alkyl; and

R_6 represents a group of formula

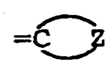
$-C \equiv C - R_{11}$ IIIa $\qquad$ $-\underset{\displaystyle R_{11}}{\underset{|}{C}} = CH_2$ IIIb

oder

 IIIc

wherein R_{11} represents hydrogen, optionally α-hydroxy substituted alkyl; alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, phenyl, phenalkyl or thienyl,

R_{12}, R_{13} and R_{14} represent, independently, hydrogen or lower alkyl, and

 represents a C_{5-8} cycloalkylidene radical optionally containing a double bond; or

b) R_1 represents a group of formula IIa to IIg as defined under a),

R_2 represents hydrogen or lower alkyl,

R_3 and R_4 together form a group $-(CH_2)_u-$, wherein u is an integer of 1 to 8, and

R_5 and R_6 have the meanings given under a).

Any lower alkyl or lower alkoxy radical has preferably 1 to 4 carbon atoms, especially 2 or 1 carbon atoms. Unless otherwise stated alkyl moieties preferably have 1 to 12 carbon atoms especially 2 to 8 carbon atoms,

particularly 2 to 6 carbon atoms and most preferably 2 to 4 carbon atoms and if bridging 1 to 4 particularly 1 or 2 carbon atoms. Any alkenyl or alkynyl radical has preferably 3 to 6 carbon atoms, especially 3 or 4 carbon atoms, e.g. allyl, propenyl or propynyl. Such alkyl, alkoxy, alkenyl and alkinyl groups can be straight-chain or branched. A preferred cycloalkylidene radical is cyclohexylidene. The term cycloalkyl is to be understood as including polycyclo groups such as bornyl or adamantyl but is preferably cyclohexyl or cyclopentyl.

Conveniently R_7 and R_8 are identical and are both hydrogen. Conveniently R_9 is hydrogen or halogen. In IIb and IIc the bond to the carbon atom to which R_2 and R_3 are attached is conveniently attached meta to X and para to the ring nitrogen, respectively. X is conveniently sulphur, imino or lower alkylamino. R_1 is preferably a radical of formula IIb, IIc or IId, or especially IIa. R_2 is preferably hydrogen. R_3 is preferably hydrogen and R_4 is conveniently alkyl. R_5 is conveniently hydrogen.

The values of p, r, s, t, u and v are conveniently chosen to produce a seven- preferably a five- or six-membered ring.

The double bond between R_6 and the nitrogen atom preferably has the trans-configuration.

Halogen stands for fluorine, chlorine or bromine, preferably chlorine or bromine.

The present invention also provides a process for the production of a compound of formula I, which comprises

a) when R_6 represents a group of formula IIIa, as defined above, (compound Ia), reacting a compound of formula IV,

$$R_2 - \underset{\substack{|\\ R_3}}{\overset{\substack{R_1\\ |}}{C}} - NH - R_4 \qquad IV$$

wherein R_1 to R_4 are as defined above, with a compound of formula V,

$$A - \overset{\substack{R_5\\ |}}{CH} - CH = CH - R_6' \qquad V$$

wherein A is a leaving group, R_5 is as defined above, and R_6' stands for a group of formula IIIa, as defined above, or

b) when R_6 represents a group of formula IIIa, wherein R_{11} represents α-hydroxyalkyl (compounds Ib), reacting a metalated compound of formula Ic,

$$R_2 - \underset{\substack{|\\ R_3}}{\overset{\substack{R_1\\ |}}{C}} - \overset{\substack{R_4\\ |}}{N} - \overset{\substack{R_5\\ |}}{CH} - CH = CH - C \equiv CH \qquad Ic$$

wherein R_1 to R_5 are as defined above, with a carbonyl compound of formula VII,

$$R_{15}.CO.CH\begin{matrix} \diagup R_{16} \\ \diagdown R_{17} \end{matrix} \qquad \text{VII}$$

wherein R_{15}, R_{16} and R_{17} represent independently hydrogen or lower alkyl, or

c) when the double bond between R_6 and the nitrogen atom is in trans configuration (compounds Id) reducing a compound of formula VIII,

$$R_2 - \overset{\displaystyle R_1}{\underset{\displaystyle R_3}{\overset{|}{\underset{|}{C}}}} - \overset{\displaystyle R_4}{\overset{|}{N}} - \overset{\displaystyle R_5}{\overset{|}{CH}} - C \equiv C - R_6 \qquad \text{VIII}$$

wherein R_1 to R_6 are as defined above, with diisobutylaluminiumhydride, or

d) when R_6 represents a group of IIIb or IIIc as defined above or a group of formula IIId,

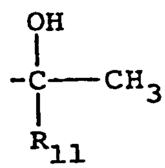
$$-C \equiv C - \underset{\displaystyle R_{15}}{\underset{|}{C}} = C\begin{matrix} \diagup R_{16} \\ \diagdown R_{17} \end{matrix} \qquad \text{IIId}$$

wherein R_{15}, R_{16} and R_{17} are as defined above (compounds Ie) splitting off water from a compound of formula

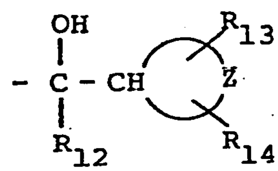
$$R_2 - \overset{\displaystyle R_1}{\underset{\displaystyle R_3}{\overset{|}{\underset{|}{C}}}} - \overset{\displaystyle R_4}{\overset{|}{N}} - \overset{\displaystyle R_5}{\overset{|}{CH}} - CH = CH - R_6''' \qquad \text{If}$$

wherein R_1 to R_5 are as defined above,

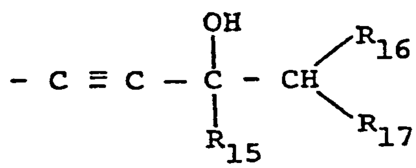
and R_6''' represents a group of formula IIIe, IIIf, or IIIg,



IIIe ;



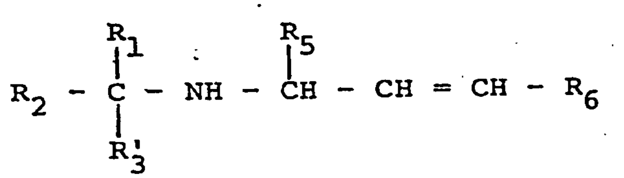
IIIf



IIIg

wherein R_{11} to R_{17} and Z are as defined above, or

e) when R_3 represents hydrogen or lower alkyl and R_4 represents C_{1-6}alkyl or C_{3-8}cycloalkyl-(C_{1-6})-alkyl (compounds Ig), introducing the group R_4' into a compound of formula IX,



IX

wherein R_1, R_2, R_5 and R_6 are as defined above,

R_3' represents hydrogen or lower alkyl, and

R_4' represents C_{1-6}alkyl or C_{3-8}cycloalkyl-(C_{1-6})-alkyl.

Process a) may be effected in conventional manner for the production of tertiary amines by condensation from analogous starting materials. The process may

be effected in an inert solvent such as a lower alkanol, e.g. ethanol, optionally in aqueous admixture, an aromatic hydrocarbon solvent, e.g. benzene or toluene, a cyclic ether, e.g. dioxane or a carboxylic acid dialkylamide solvent, e.g. dimethylformamide. The reaction temperature is conveniently from room temperature to the boiling temperature of the reaction mixture, preferably room temperature. The reaction is conveniently effected in the presence of an acid binding agent, such as an alkali metal carbonate, e.g. sodium carbonate. The leaving group A is conveniently iodine or preferably chlorine or bromine, or an organic sulphonyloxy group having 1 to 10 carbon atoms, e.g. alkylsulphonyloxy, preferably having 1 to 4 carbon atoms such as mesyloxy, or alkylphenylsulphonyloxy preferably having 7 to 10 carbon atoms such as tosyloxy.

Process b) may be effected in conventional manner, for example by metalating the compound of formula Ic, e.g. with butyllithium in an inert solvent such as an ether e.g. tetrahydrofuran and subsequently reacting the metalated compound of formula Ic, thus obtained, preferably without isolation with a compound of formula VII.

The reduction with diisobutylaluminium hydride (DIBAH) according to process c) is preferably carried out in an inert solvent e.g. in an aromatic hydrocarbon such as toluene or benzene and at room temperature or raised temperature e.g. 35 to 40°C.

The splitting-off of water according to process d) can be carried out with a suitable agent such as an inorganic acid, e.g. hydrochloric or sulphuric acid, an organic acid, e.g. methanesulphonic acid, benzenesulphonic acid or p-toluenesulphonic acid or an inorganic or organic acid anhydride or -halide e.g. $POCl_3$ in an inert solvent. An excess of an acid halide if used can act as reaction medium whereby the reaction is carried out in the presence of an acid binding agent such as a tertiary amine, e.g. a trialkylamine or a tertiary amine, e.g. a trialkylamine or pyridine. Reaction temperatures vary according to reaction conditions and lie for example between -10 and 180°C. The splitting-off of water can also be carried out with the help of polyphosphoric acid at temperatures between 80 and 120°C whereby inorganic acids such as phosphoric acid, organic acids such as acetic acid or an excess of polyphosphoric acid can serve as solvent.

Process e) may be effected in manncer conventional for the "alkylation" of secondary amines (the term "alkylation" being used here to denote introduction of any of the hydrocarbyl groups R_4), for example by direct "alkylation" with an "alkylating" agent, for example a halide or sulphate, or by reductive alkylation, in particular by reaction with an appropriate aldehyde and subsequent or simultaneous reduction. Reductive "alkylation"

is suitably effected by reacting a compound of formula IX in an inert organic solvent, such as a lower alkanol, e.g. methanol, and at an elevated temperature, in particular at the boiling temperature of the reaction mixture with the corresponding aldehyde. The subsequent reduction may be effected with, for example, a complex metal hydride reducing agent, e.g. $NaBH_4$ or $LiAlH_4$. The reduction may also be effected simultaneously to the alkylation, for example by use of formic acid which may serve both as reducing agent and as a reaction medium. The reaction is preferably carried out at raised temperature, in particular at the boiling point of the reaction mixture.

Free base forms of the compounds of formula I may be converted into salt forms and vice versa. Suitable acid addition salts are e.g. hydrochloride, hydrogen fumarate or naphthaline-1,5-disulphonate.

The compounds of the formula I and their intermediates can be obtained in the form of isomeric mixtures of the various cis/trans isomers which can be separated according to established methods. Alternatively, isomers of the compounds can be obtained by using the appropriate isomer of the starting material. Unless otherwise stated the compounds are always to be understood as being mixtures of these isomers.

The starting materials of formula IV are in part new and can be prepared by reacting in conventional

manner a compound of formula X,

$$R_2 - \underset{\displaystyle R_3}{\overset{\displaystyle R_1}{\underset{|}{\overset{|}{C}}}} - \text{Hal} \qquad\qquad \text{X}$$

with a compound of formula XI,

$$R_4 - NH_2 \qquad\qquad \text{XI}$$

wherein in the formulae X and XI R_1 to R_4 are as defined above and Hal stands for halogen.

The starting materials of formula V are in part new and can be prepared by reacting a compound of formula XII,

$$R_6' \, H \qquad\qquad \text{XII}$$

according to the following scheme

$$\underset{\text{XII}}{R_6' \, H} \longrightarrow \underset{\text{XIII}}{R_6'^{\ominus} \; Me^{\oplus}} + \underset{\text{XIV}}{R_5.CO.CH{=}CH_2} \longrightarrow$$

$$\longrightarrow \underset{\text{XV}}{R_6' - \underset{\displaystyle OH}{\overset{\displaystyle R_5}{\underset{|}{\overset{|}{C}}}} - CH = CH_2} \xrightarrow{+\ HA} V$$

whereby R_6', R_5 and A are as defined above and $Me^{\oplus}$ represents a metal cation.

The starting materials of formula VIII are new and can be prepared a') by subjecting a compound of formula IV, defined above, and compounds of formulae XVI and XVII

$$HC \equiv C{-}R_6 \quad \text{and} \quad R_5CHO$$

XVI XVII

to a Mannich reaction or

b') in the case when R_6 represents a group of formula IIIa as defined above by reacting a compound of formula IV as defined above with a compound of formula XVIII

$$HC \equiv C - \overset{\displaystyle R_5}{\overset{|}{C}}H - A \qquad \text{XVIII}$$

to give a compound of formula XIX,

$$R_2 - \underset{\displaystyle R_3}{\underset{|}{\overset{\displaystyle R_1}{\overset{|}{C}}}} - \overset{\displaystyle R_4}{\overset{|}{N}} - \overset{\displaystyle R_5}{\overset{|}{C}}H - C \equiv CH \qquad \text{XIX}$$

and subjecting this to a Cadiot-Chodkiewicz coupling reaction with Cu^+ and a compound of formula XX,

$$R_6' \text{ Hal} \qquad \text{XX}$$

or c') when R_6 represents a group of formula IIIb as defined above splitting off water from a compound of formula XXI,

$$R_2 - \underset{R_3}{\overset{R_1}{\overset{|}{\underset{|}{C}}}} - \overset{R_4}{\overset{|}{N}} - \overset{R_5}{\overset{|}{CH}} - C \equiv C - \underset{R_{11}}{\overset{OH}{\overset{|}{\underset{|}{C}}}} - CH_3 \qquad \text{XXI}$$

whereby in the formulae XVI to XXI R_1 to R_6, R_6', R_{11}, A and Hal are as defined above.

The starting materials of formula IX are new and can be prepared for example by reacting a compound of formula XXII,

$$R_2 - \underset{R_3'}{\overset{R_1}{\overset{|}{\underset{|}{C}}}} - NH_2 \qquad \text{XXII}$$

with a compound of formula XXIII

$$O = \overset{R_5}{\overset{|}{C}} - CH = CH - R_6 \qquad \text{XXIII}$$

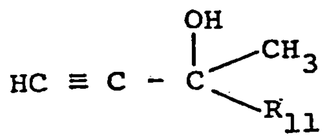
to give a compound of formula XXIV

$$R_2 - \underset{R_3'}{\overset{R_1}{\overset{|}{\underset{|}{C}}}} - N = \overset{R_5}{C} - CH = CH - R_6 \qquad \text{XXIV}$$

and reducing this e.g. with a complex hydride such as $NaBH_4$, whereby in the formulae XXII to XXIV R_1, R_2, R_3', R_5 and R_6 are as defined above.

Compounds of formula XXI can be prepared

a") by subjecting a compound of formula IV as defined above, a compound of formula XVII as defined above, and a compound of formula XXV,



XXV

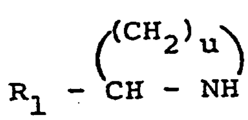
to a Mannich reaction, or

b") metalating a compound of formula XIX, as defined above, and reacting the metal compound thus obtained with a carbonyl compound of formula XXVI,

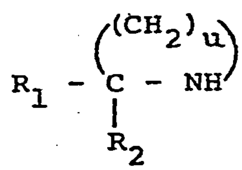
$$CH_3.CO.R_{11} \qquad \text{XXVI}$$

whereby in the formulae XXV and XXVI R_{11} is as defined above.

The compounds of formulae IVa and IVb

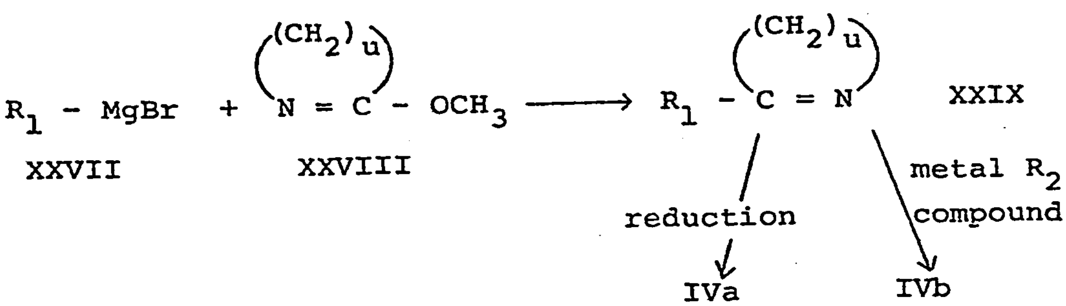


IVa ;



IVb

can be prepared according to the following scheme



whereby in the formulae IVa, IVb and XXVII to XXIX R_1, R_2 and u are as defined above.

The starting materials of formula If wherein R_6''' represents a group of formula IIIe or IIIf as defined above are new and can be prepared by reduction with $LiAlH_4$ of a compound of formula XXIa,

$$\begin{array}{ccccccccc} & & R_1 & & R_4 & & R_5 & & \\ & & | & & | & & | & & \\ R_2 & - & C & - & N & - & CH & - & C \equiv C - R_6''' \\ & & | & & & & & & \\ & & R_3 & & & & & & \end{array} \qquad \text{XXIa}$$

wherein R_1 to R_5 are as defined above and R_6''' represents a group of formula IIIe or IIIf as defined above.

Compounds of formula XX are in part new and can be prepared by reacting a compound of formula XII, as defined above, with butyllithium and a halogen.

The new compounds of formulae IV, V, VII, IX XX and If also form part of the invention. The remaining intermediate compounds are either known or can be prepared according to known methods or as hereinbefore described.

The compounds of formula I exhibit chemotherapeutic activity. In particular, they exhibit antimycotic activity, as indicated <u>in vitro</u> in various families and types of mycetes, including Trichophyton spp, Aspergillus spp Microsporum spp and Sporotrychium schenkii and Candida spp at concentrations of, for example 0.01 to 100 µg/ml, and <u>in vivo</u> in the experimental skin mycosis model in guinea pigs. In this model, guinea pigs are infected by subcutaneous applications of Trichophyton Quinckeanum. The

test substance is administered daily for 7 days beginning 24 hours after the infection either by local application by rubbing the test substance (taken up in polyethylene glycol) on the skin surface, or perorally or sub-cutaneously, the test substance being administered as a suspension. The activity is shown on local application at concentrations of for example 0.01 to 5%. The oral activity is shown _in vivo_ in the guinea-pig - Trichophytosis model at dosages of, for example 2 to 70 mg/kg.

The compounds are therefore indicated for use as anti-mycotic agents in particular against dermatophytes. An indicated daily dose is from 70 to 2000 mg. If desired, this may be administered in divided doses 2 to 4 times a day in unit dosage form containing from about 17.5 mg to about 1000 mg or in sustained release form. The invention therefore also concerns a method of treating diseases or infections caused by mycetes using a compound of formula I and also compounds of formula I for use as chemotherapeutic agents e.g. as antimycotic agents and for use in the treatment of the human or animal body by therapy.

The compounds may be used in free base form or in the form of chemotherapeutically acceptable acid addition salts. Such salt forms exhibit the same order of activity as the free base forms. Suitable salt forms are e.g. hydrochloride, hydrogen fumarate or naphthaline-1,5-disulphonate.

The compounds may be admixed with conventional chemotherapeutically acceptable diluents and carriers, and, optionally, other excipients and administered in such forms as tablets or capsules. The compounds may alternatively be administered topically in such conventional forms as ointments or creams or parenterally. The concentrations of the active substance will of course vary depending on the compound employed, the treatment desired and the nature of the form etc. In general, however, satisfactory results are obtained e.g. in topical application forms at concentrations of from 0.05 to 5, in particular 0.1 to 1 wt %.

Such compositions also form part of the invention.

Examples of preferred compound groups are

(i) compounds of formula I wherein R_{11} represents alkyl, alkenyl, alkynyl, cycloalkylalkyl, phenyl or phenalkyl and all other substituents are as defined under formula I;

(ii) compounds of formula I wherein

a) R_1 represents a group of the formula IIa, IIb, IIe,
R_2 represents hydrogen,
R_3 represents hydrogen,
R_4 represents lower alkyl,
R_5 represents hydrogen or lower alkyl,
or R_3 and R_4 together form a group $-(CH_2)_u-$ or

b) wherein R_1 and R_2 together represent a group of the formula IIh,

R_3 represents hydrogen,

R_4 represents lower alkyl,

R_5 represents lower alkyl and

R_6 is as hereinbefore defined,

whereby within these groups R_6 is preferably a group of formula IIa as hereinbefore defined and/or R_1 is preferably a group of formula IIa.

Preferred meanings of the substituents in the compounds of the formula I are such as set out hereinbefore.

Compounds of formula I are generally preferred wherein the double bond between R_6 and the nitrogen atom is in trans-configuration.

Particularly preferred individual compounds are: N-methyl-N-(1-naphthylmethyl)-non-2(trans)-en-4-ynyl-1-amine and N-methyl-N-(1-naphthylmethyl)-6,6-dimethyl-hept-2(trans)-en-4-ynyl-1-amine, and their hydrochlorides.

The following Examples illustrate the invention whereby all temperatures are in degrees centigrade.

EXAMPLE 1:

trans-N-(3-Benzo[b]thiophenemethyl)-N-methyl-non-2-en-ynyl-1-amine and cis-N-(3-Benzo[b]thiophenemethyl)-N-methyl-non-2-en-ynyl-1-amine [process a)]

12 g 1-Bromo-2-nonen-4-yne (cis/trans mixture) are added dropwise to a mixture of 10.5 g N-(3-Benzo[b]-thiophenemethyl)-N-methylamine, 8.2 g K_2CO_3 and 100 ml dimethylformamide and stirred overnight. The reaction mixture is filtered and the solvent removed under vacuum. The residue is partitioned between ether and saturated aqueous $NaHCO_3$, the organic phase dried, concentrated under vacuum and chromatographed over kieselgel using toluene/ethylacetate 4:1 as eluant. The trans isomer is eluted first followed by the cis isomer. Both are oils.

EXAMPLE 2:

trans-N-Methyl-N-(1-naphthylmethyl)-6-hydroxy-6-methyl-hept-2-en-4-ynyl-1-amine [process b)]

10.7 ml of a 15% butyllithium solution in hexane are added dropwise to 3g of trans N-methyl-N-(1-naphthylmethyl)pent-2-en-4-ynyl-1-amine in absolute tetrahydrofuran and reacted after 30 minutes with a solution of 1.79 g of acetone. The reaction mixture is stirred for 24 hours at room temperature, poured onto ice and extracted

with chloroform. The organic phase is washed, dried and concentrated under vacuum. After chromatography over kieselgel (eluant toluene/ethyl acetate 4:1) the title compound is obtained as an oil.

EXAMPLE 3:

a) trans-N-Methyl-N-(1-naphthylmethyl)-non-2-en-4-ynyl-1-amine [process c)]

72 ml of a 1.2M solution of DIBAH in toluene are added dropwise to a solution of 5g N-methyl-N-(1-naphthylmethyl)-2,4-nonadiynyl-1-amine in dry toluene and the resulting mixture stirred under protective gas overnight at 40° and then for 24 hours at room temperature.

The excess reagent is broken down with 2N NaOH under cooling and the reaction mixture extracted with ether. The organic phase is dried, concentrated under vacuum and chromatographed over kieselgel (eluant - toluene/ethyl-acetate 95:5). The title substance is isolated as an oil.

b) Hydrochloride salt

The compound from a) is converted to its hydrochloride in conventional manner e.g. by treating with 4N ethanolic HCl and melts after recrystallisation at 118-121°C.

EXAMPLE 4:

N-Methyl-N-(1-naphthylmethyl)-deca-2(trans),6(cis)-dien-4-ynyl-1-amine

1g trans-N-Methyl-N-(1-naphthylmethyl)-6-hydroxy-dec-2-en-4-ynyl-1-amine are refluxed under a water separator with 570 mg p-toluenesulphonic acid (monohydrate) in benzene. The mixture is cooled after 2 hours, the organic phase shaken a number of times with saturated aqueous $NaHCO_3$, dried and concentrated under vacuum. The residue is chromatographed over kieselgel (eluant - toluene/ethylacetate 9:1) to give the title product.

EXAMPLE 5:

N-Methyl-N-(1-naphthylmethyl)-4-cyclohexyl-2-(trans)-4-pentadienyl-1-amine (A) and N-Methyl-N-(1-naphthylmethyl)-4-cyclohexylidenyl-2-(trans)-pentenyl-1-amine (B)

1g N-Methyl-N-(1-naphthylmethyl)-4-hydroxy-4-cyclohexyl-2-pentenyl-1-amine is refluxed under a water separator with 570 mg p-toluenesulphonic acid (monohydrate) in benzene. The mixture is cooled after 2 hours, the organic phase shaken a number of times with saturated aqueous $NaHCO_3$, dried and concentrated under vacuum. The residue is chromatographed over kieselgel (eluant - toluene/ethyl acetate 9:1) to obtain first title product (A) followed by title product (B) as oils.

EXAMPLE 6:

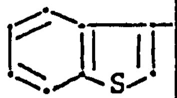
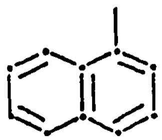
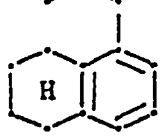
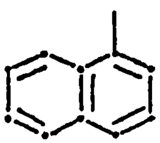
trans-N-Methyl-N-(1-naphthylmethyl)-4-cyclohexylidenyl-2-buten-yl-amine [process e)]

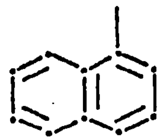
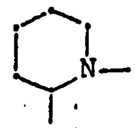
3g (1-Naphthylmethyl)methylamine and 2.86g 4-cyclohexylidenyl-2-butenal are stirred in ether together with a 4 Å molecular sieve. The reaction mixture is filtered and concentrated under vacuum. The residue is taken up in methanol, treated with 800 mg $NaBH_4$ and stirred for 2 hours at room temperature.

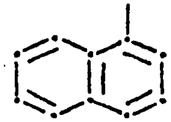
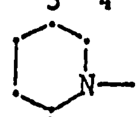
The reaction mixture containing the secondary amine thus obtained is taken directly for reductive methylation. 8 ml 37% aqueous formaldehyde solution are added and refluxed for 1 hour. The mixture is then treated under ice-cooling with 3.6g $NaBH_4$ and stirred for 16 hours at room temperature. The resulting mixture is concentrated under vacuum, the residue partitioned between saturated $NaHCO_3$ and ethyl acetate and the organic phase dried and concentrated. The title substance is obtained by chromatography over kieselgel (eluant - toluene/ethyl acetate 4:1) as an oil.

The following compounds of formula I can be obtained in an analogous manner.

TABLE I

xample	R_1	R_2	R_3	R_4	R_5	R_6	Conf.	Physical data	Proc.
7		H	H	CH_3	H	$-C{\equiv}C-(CH_2)_3-CH_3$	trans	oil	c, e
8	- " -	H	H	CH_3	H	- " -	cis	oil	e
9		H	H	CH_3	H	- " -	cis	oil	a, e
10		H	H	CH_3	H	- " -	trans	oil	a,c,e
11	- " -	H	H	CH_3	H	- " -	cis	oil	a, e
12		H	H	CH_3	H	- " -	trans	oil	a,c,e
13	- " -	H	H	CH_3	H	- " -	cis	oil	a, e
14		H	H	CH_3	H	$- C \equiv CH$	trans	mp (hydrochloride) 150-155°	a,c,e

e	R_1	R_2	R_3	R_4	R_5	R_6	Conf.	Physical data	Proc.
		H	R_3+R_4+N 		H	$-C\equiv CH$	trans	mp (hydrochloride) 150-155°	a,c
	- " -	H	H	CH_3	H	$-C\equiv C-C(CH_3)_3$	trans	m.p. (hydrochloride) 199-202° (crystal invertion above 135°)	a,c,e
	- " -	H	H	CH_3	H	- " -	cis	oil	a, e
	- " -	H	H	CH_3	H	$-C\equiv C-C_6H_5$	trans	oil	a,c,e
	- " -	H	H	CH_3	H	- " -	cis	oil	a, e
	- " -	H	H	CH_3	H	$-C\equiv C-CH(CH_3)(C_2H_5)$	trans	m.p. (hydrochloride) 160-162°	a,c,e
	- " -	H	H	CH_3	H	- " -	cis	oil	a,e
	- " -	H	H	CH_3	H	$-C\equiv C-CH_2-CH(CH_3)_2$	trans	m.p. (hydrochloride) 124-126°	a,c,e
	- " -	H	H	CH_3	H	- " -	cis	oil	a, e
	- " -	H	H	CH_3	H	$-C\equiv C-$ 	trans	oil	a,c,e

Example	R_1	R_2	R_3	R_4	R_5	R_6	Conf.	Physical data	Proc.
5		H	H	CH_3	H	$-C{\equiv}C-C(OH)(CH_3)-CH_3$	trans	oil	c,e
6	- " -	H	H	CH_3	H	$-C{\equiv}C-C(OH)(C_2H_5)-C_2H_5$	trans	oil	b,c,e
[illegible]	- " -	H	H	CH_3	H	$-C{\equiv}C-CH(OH)-(CH_2)_3-CH_3$	trans	oil	b,c,e
28	- " -	H	H	CH_3	H	$-C{\equiv}C-C(OH)(C_2H_5)-CH_3$	trans	oil	b,c,e
29	- " -	H	H	CH_3	H	$-C{\equiv}C-C(OH)(C(CH_3)_3)-CH_3$	trans	oil	b,c,e
30	- " -	H	H	CH_3	H	$-C{\equiv}C-(CH_2)_3-CH_3$	trans	mp (hydrochloride 118-121°	a, e
31	- " -	H	H	CH_3	H	$-C{\equiv}C-(CH_2)_2-CH_3$	trans	oil	a,c,e
[illegible]	- " -	H	H	CH_3	H	$-C{\equiv}C-(CH_2)_4-CH_3$	trans	oil	a,c,e
33	- " -	H	H	CH_3	H	$-C{\equiv}C-(CH_2)_5-CH_3$	trans	oil	a,c,e
34	- " -	H	R_3+R_4+N 		H	$-C{\equiv}C-(CH_2)_2-CH_3$	trans	oil	a,c
	"	"	- " -		H	$-C{\equiv}C-(CH_2)_3-CH_3$	trans	oil	a,c

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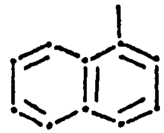
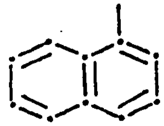
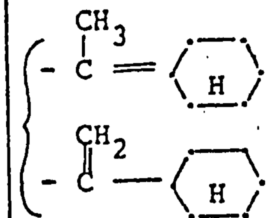
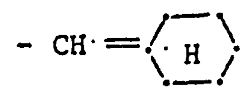
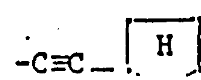
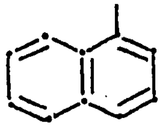
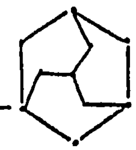
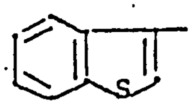
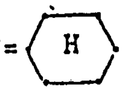
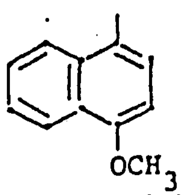
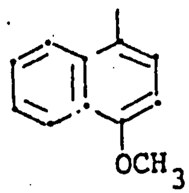
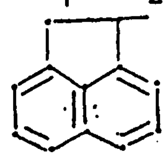
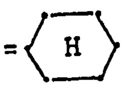
	R1	R2	R3	R4	R5	R6	Conf.	Physical data	Proc.
		H	H	CH_3	H	$-C{\equiv}C-CH{=}CH-(CH_2)_2-CH_3$	trans	oil	a,c,e
	- " -	H	H	CH_3	H	$-C{\equiv}C-C(C_2H_5){=}CH.CH_3$	trans	oil	a,c,d,e
	- " -	H	H	CH_3	H	$-C{\equiv}C-C(CH_3){=}CH.CH_3$	trans	oil	a,c,d,e
	- " -	H	H	CH_3	H	$-C{\equiv}C-C(C(CH_3)_3){=}CH_2$	trans	oil	a,c,d,e
	- " -	H	H	CH_3	H	$-C(C_6H_5)=CH_2$	trans	oil	c,d,e
	- " -	H	H	CH_3	H	$-C(CH_2.CH(CH_3)CH_3)=CH_2$	trans	oil	c,d,e
	- " -	H	H	CH_3	H	$-C((CH_2)_3-CH_3)=CH_2$	trans	oil	c,d,e
	- " -	H	H	CH_3	H	$-C(C(CH_3)_3)=CH_2$	trans	oil	c,d,e

Example	R_1	R_2	R_3	R_4	R_5	R_6	Conf.	Physical data	Proc.
44		H	H	CH_3	H		trans	oil	c,e
							trans	oil	c,e
45	- " -	H	H	CH_3	H		trans	oil	c,d
46	- " -	H	H	CH_3	H	$-C{\equiv}C-CH_2OH$	trans	oil	b,c,e
47	- " -	H	H	CH_3	CH_3	$-C{\equiv}C-(CH_2)_3-CH_3$	trans	oil	a,c,e
48	- " -	H	H	CH_3	CH_3	- " -	cis	oil	a,e
49	- " -	H	H	CH_3	H	$-C{\equiv}C-C(CH_3)_2-C_2H_5$	trans	oil	a,c,e
50	- " -	H	H	CH_3	H	- " -	cis	oil	a,e
[illegible]	- " -	"	"	CH_3	H		trans	oil	a,c,e

R_1	R_2	R_3	R_4	R_5	R_6	Conf.	Physical data	Proc.
	H	H	CH_3	H	-C≡C— 	cis	oil	a,e
- " -	H	H	CH_3	H	-C≡C— 	trans	oil	a,c,e
- " -	H	H	CH_3	H	- " -	cis	oil	a,e
	H	H	CH_3	H	-CH= 	trans	oil	c,d,e
	H	H	CH_3	H	$-C\equiv C-C(CH_3)_3$	cis	oil	a,c,e

xample	R_1	R_2	R_3	R_4	R_5	R_6	Conf.	Physical data	Proc.
57		H	H	CH_3	H	$-C\equiv C-C(CH_3)_3$	cis	oil	a,e
58	$R_1 + R_2$ 		H	CH_3	H	$-CH=$ 	trans	oil	c,d,e
59	- " -		H	CH_3	H	$-C\equiv C-C(CH_3)_3$	trans	oil	a,c,e

In the following table NMR data are given. Data comprises peaks in ppm relative to TMS as standard in $CDCL_3$. Types of peaks are

m = multiplet

dt = double triplet

dm = double multiplet

s = singlet

d = doublet

t = triplet

ps.t = pseudo triplet

dd = double doublet

dbr = double broad

br = broad

qua = quartet

mbr = multiple broad

sext = sextuplet

ddd = double double doublet

sbr = single broad

Example	Isomer	Spectrum
1, 7	trans	δ = 7.7-8.0 (m, 2H); 7.15-7.45 (m, 4H); 6.14 (dt, J=16 and 2 x 6.5 Hz, 1 olef. H); 6.65 (dm, J=16 Hz, 1 olef. H); 3.72 (s, 2H); 3.10 (d, J=6.5 Hz, 2H); 2.3 (m, 2H); 2.24 (s, 3H); 1.2-1.7 (m, 4H); 0.9 (ps.t., 3H).
1,8	cis	δ = 7.7-8.0 (m, 2H); 7.15-7.45 (m, 4H); 6.0 (dt, J=11 and 2 x 6.5 Hz, 1 olef. H); 5.64 (dm, J=11 Hz, 1 olef. H); 3.66 (s, 2H); 3.35 (d, J=6.5 Hz, 2H); 2.34 (m, 2H); 2.28 (s, 3H); 1.2-1.7 (m, 4H); 0.9 (ps.t., 3H).
9	cis	δ = 8.2-8.4 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.05 (dt, J=10.8 + 2 x 7 Hz, 1 olef. H); 5.65 (dm, J=10.8 Hz, 1 olef. H); 3.92 (s, 2H); 3.38 (dd, J=7 u. 1.5 Hz, 2H); 2.34 (m, 2H); 2.25 (s, 3H); 1.2-1.8 (m, 4H); 0.94 (m, 3H).
10	trans	δ = 6.9-7.2 (m, 3H); 6.12 (dt, J=16 and 2 x 6.5 Hz, 1 olef. H); 5.64 (dm, J=16 Hz, 1 olef. H); 3.4 (s, 2H); 3.05 (d, J=6.5 Hz, 2H); 2.7-2.9 (m, 4H); 2.2-2.4 (m, 2H); 2.18 (s, 3H); 1.65-1.9 (m, 4H); 1.3-1.7 (m, 4H); 0.92 (m, 3H).
11	cis	δ = 6.85-7.2 (m, 3H); 5.97 (dt, J=11 and 6.5 Hz, 1 olef. H); 5.60 (dm, J=11 Hz, 1 olef. H); 3.45 (s, 2H); 3.30 (d, J=6.5 Hz, 2H); 2.7-2.9 (m, 4H); 2.2-2.4 (m, 2H); 2.22 (s, 3H); 1.7-1.9 (m, 4H); 1.3-1.7 (m, 4H); 0.95 (m, 3H).

Example	Isomer	Spectrum
12	trans	δ = 7.1-7.8 (m, 5H); 6.14 (dt, J=16 and 2 x 6.5 Hz, 1 olef. H); 5.65 (dm, J= 16 Hz, 1 olef. H); 3.63 (s, 2H); 3.1 (d, J=6.5 Hz, 2H); 2.2-2.4 (m, 2H); 2.25 (s, 3H); 1.2-1.7 (m, 4H); 0.9 (m, 3H).
13	cis	δ = 7.1-7.8 (m, 5H); 6.0 (dt, J=11 and 2 x 6.5 Hz, 1 olef. H); 5.64 (dm, J= 11 Hz, 1 olef. H); 3.66 (s, 2H); 3.35 (d. J=6.5 Hz, 2H); 2.2-2.4 (m, 2H); 2.30 (s, 3H); 1.2-1.7 (m, 4H); 0.9 (m, 3H).
16	trans	δ = 8.2-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.18 (dt, J=17 and 2x7 Hz); 5.65 (dm, J=17 Hz, 1H); 3.9 (s, 2H); 3.12 (dd, J= 7 u. 1 Hz, 2H); 2.22 (s, 3H); 1.25 (s, 9H).
17	cis	δ = 8.2-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.03 (dt, J=11 and 2 x 6.5 Hz, 1H); 5.65 (dbr, J=11 Hz, 1H); 3.92 (s, 2H); 3.38 (d, J=6.5 Hz, 2H); 2.26 (s, 3H); 1.27 (s, 9H).
18	trans	δ = 8.2-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.2-7.6 (m, 9H); 6.36 (dt, J=16 and 2 x 6.5 Hz, 1H); 5.9 (dm, J=16 Hz, 1H); 3.94 (s, 2H); 3.22 (d, J=6.5 Hz, 2H); 2.28 (s, 3H).
19	cis	δ = 8.2-8.4 (m, 1H); 7.7-7.9 (m, 2H); 7.2-7.6 (m, 9H); 6.20 (dt, J=11 and 2 6.5 Hz, 1H); 5.85 (d, J=11 Hz, 1H); 3.98 (s, 2H); 3.50 (d, J=6.5 Hz, 2H); 2.30 (s, 3H).

Example	Isomer	Spectrum
20	trans	δ = 8.2-8.4 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.20 (dt, J=16 and 2 x 6.5 Hz, 1H); 5.80 (dm, J=16 Hz, 1H); 3.90 (s, 2H); 3.14 (d, J=6.5 Hz, 2H); 2.5 (m, 1H); 2.24 (s, 3H); 1.2-1.7 (m, 2H); 1.18 (d, J=7 Hz, 3H); 1.0 (t, J=7 Hz, 3H).
21	cis	δ = 8.2-8.4 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.05 (dt, J=11 and 2 x 6.5 Hz, 1H); 5.67 (dm, J=11 Hz, 1H); 3.94 (s, 2H); 3.40 (d, J=6.5 Hz, 2H); 2.55 (m, 1H); 2.28 (s, 3H); 1.2-1.8 (m, 2H); 1.20 (d, J=7 Hz, 3H); 1.02 (t, J=7 Hz, 3H).
22	trans	δ = 8.2-8.35 (m, 1H); 7.65-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.20 (dt, J=16 and 2 x 6.5 Hz, 1H); 5.68 (dm, J=16 Hz, 1H); 3.88 (s, 2H); 3.13 (d, J=6.5 Hz, 2H); 2.22 (s, 3H); 2.2 (m, 2H); 1.6-2.1 (m, 1H); 1.0 (d, J=7 Hz, 6H).
23	cis	δ = 8.2-8.4 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.04 (dt, J=12 and 2 x 7 Hz, 1H); 5.65 (dbr, J=12 Hz, 1H); 3.90 (s, 2H); 3.38 (d, J=7 Hz, 2H); 2.24 (s, 3H); 2.2 (m, 2H); 1.6-2.0 (m, 1H); 1.0 (d, J=7 Hz, 6H).
24	trans	δ = 8.2-8.4 (m, 1H); 7.65-7.9 (m, 2H); 7.3-7.6 (m, 4H); 7.15-7.3 (m, 2H); 6.95 (m, 1H); 6.36 (dt, J=16 u. 2 x 6 Hz, 1H); 5.9 (dbr, J=16 Hz, 1H); 3.92 (s, 2H); 3.20 (d, J=6 Hz, 2H); 2.28 (s, 3H).

Example	Isomer	Spectrum
2,25	trans	δ = 8.15-8.35 (m, 1H); 7.6-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.22 (dt, J=16 and 2 x 6.5 Hz, 1H); 5.67 (dt, J=16 and 2 x 1.5 Hz, 1H); 3.88 (s, 2H); 3.13 (dd, J=6.5 u. 1.5 Hz); 2.22 (s, 3H); 2.15 (br. -OH); 1.5 (s, 6H).
26	trans	identical with Ex. 2,25 except δ = 1.8 (br, OH); 1.65 (qua, J=8 Hz, 4H); 1.0 (t, J=8 Hz, 6H).
27	trans	δ = 8.2-8.35 (m, 1H); 7.6-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.26 (dt, J=16 and 2 x 6 Hz, 1H); 5.7 (dm, J=16 Hz, 1H); 4.46 (mbr, 1H); 3.90 (s, 2H); 3.15 (d, J=6 Hz, 2H); 2.25 (s, 3H); 2.0 (br, OH); 1.2-1.8 (m, 6H); 0.9 (m, 3H).
28	trans	δ = 8.15-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.25 (dt, J=16 and 2 x 6.5 Hz, 1 olef. H); 5.70 (dbr, J=16 Hz, 1H); 3.9 (s, 2H); 3.14 (d, J=6.5 Hz, 2H); 2.24 (s, 3H); 2.1 (br, OH); 1.72 (qua, J=7 Hz, 2H); 1.50 (s, 3H); 1.04 (t, J = 7 Hz, 3H).
29	trans	δ = 8.15-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.22 (dt, J=16 and 2 x 6.5 Hz, 1H); 5.70 (dm, J=16 Hz, 1H); 3.9 (s, 2H); 3.14 (d, J=6.5 Hz, 2H); 2.24 (s, 3H); 1.95 (m, OH); 1.46 (s, 3H); 1.06 (s, 9H).

Example	Isomer	Spectrum
3,30	trans	δ = 8.2-8.35 (1 arom. H); 7.7-7.9 (2 arom. H); 7.3-7.6 (4 arom. H); 6.17 (dt, 1 olef. H, J=16 + 2 x 6.5 Hz); 5.67 (d, 1 olef. H, J=16 Hz); 3.89 (s, 2H); 3.13 (d, 2H, J=6.5Hz); 2.21 (s, 3H); 2.2-2.4 (m, 2H); 1.2-1.8 (4H); 0.8-1.05 (m, 3H).
31	trans	identical with Ex. 3,30 except: δ = 2.28 (t, 2H); 1.55 (sext., 2H); 1.0 (t, 3H).
32	trans	identical with Ex. 3,30 except: δ = 1.2 - 1.8 (m, 6H).
33	trans	identical with Ex. 3,30 except: δ = 1.2 - 1.8 (m, 8H).
34	trans	δ = 8.5 (br, 1H); 7.3-7.9 (m, 6H); 6.02 (ddd, J=5, 8 + 16 Hz, 1H); 5.46 (dbr. J=16 Hz, 1H); 3.80 (br, 1H); 3.1-3.35 (m, 2H); 2.52 (dd, 8 + 14 Hz, 1H);2.0-2.35 (m, 3H); 1.6-2.0 (m, 6H); 1.54 (sext., J=7 Hz, 2H); 0.97 (t, J=7 Hz, 3H).
35	trans	identical with Ex. 34 except: δ = 1.3-1.7 (m, 4H); 0.9 (ps.t, 3H).
4,36	trans	δ = 8.2-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.26 (dt, J=15.5 + 2x 6.5 Hz, 1H); 5.9 (dt, J=11 + 2x7 Hz); 5.85 (d, J=15.5 Hz, 1H); 5.58 (dbr, J= 11 Hz); 3.92 (s, 2H); 3.18 (d, J= 6.5 Hz, 2H); 2.35 (t, 2H); 2.26 (s, 3H); 1.2-1.7 (m, 2H); 0.95 (ps.t. 3H).

Example	Isomer	Spectrum
37	trans	δ = 8.15-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.25 (dt, J=16 + 6 Hz, 1H); 5.86 (d, J=16 Hz, 1H); 5.70 (t, J= 7 Hz, 1H); 3.94 (s, 2H); 3.20 (d, J=6 Hz, 2H); 2.26 (s, 3H); 2.16 (qua, J=8 Hz, 2H); [1.8 (d, J=7 Hz) und 1.7 (d, J=7 Hz); Σ 3H, in ratio 6/1]; 1.06 (t, 3H).
38	trans	δ = 8.2-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.30 (dt, J=16 + 2x6 Hz, 1H); 5.86 (d,J=16 Hz, 1H); 5.75 (m, 1H); 3.92 (s, 2H); 3.18 (d, J=6 Hz, 2H); 2.26 (s, 3H); 1.87 (s, 3H); 1.8 u. 1.7 (2 d, 3H).
39	trans	δ = 8.2-8.4 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.28 (dt, J=16 + 2x6.5 Hz, 1H); 5.84 (dm, J=16 Hz, 1H); 5.30 (m, $=C\langle^{H}_{H}$); 3.92 (s, 2H); 3.18 (d, J= 6.5 Hz, 2H); 2.26 (s, 3H); 1.18 (s, 9H).
5,44 A	trans	δ = 8.2-8.35 (1 arom. H); 7.7-7.9 (2 arom. H); 7.3-7.6 (4 arom. H); 6.22 (d, 1 olef. H, J=16 Hz); 5.93 (dt, 1 olef. H, J=16 + 2 x 6.5 Hz); 4.87 u. 4.83 ($=C\langle^{H}_{H}$); 3.90 (s, 2H); 3.19 (d, 2H, J=6.5 Hz); 2.25 (s, 3H); 1.0-2.4 (11 H, Cyclohexyl).
B	trans	δ = 8.2-8.35 (1 arom. H); 7.7-7.9 (2 arom. H); 7.3-7.6 (4 arom. H); 6.79 (d, 1 olef. H, J=16 Hz); 5.80 (dt, 1 olef. H, J=16 + 2 x 6.5 Hz); 3.92 (s, 2H); 3.24 (d, 2H, J=6.5 Hz); 2.2-2.5 (m, 4H); 2.26 (s, 3H); 1.88 (s, 3H), 1.58 (br, 6H).

Example	Isomer	Spectrum
40	trans	δ = 8.15-8.30 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 9H); 6.51 (d, J=18 Hz, 1H); 5.82 (dt, J=18 + 2 x 7.5 Hz, 1H); [5.26 (sbr, 1H) + 5.14 (d, J=2 Hz, 1H) $=C\langle^{H}_{H}$]; 3.88 (s, 2H); 3.20 (d, J=7.5 Hz, 2H); 2.22 (s, 3H).
41	trans	δ = 8.2-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.24 (d, J=16 Hz, 1 olef. H); 5.85 (dt, J=16 + 2 x 6.5 Hz, 1 olef. H); 4.95 (dd, J=11 + 2 Hz, 2 olef. H); 3.9 (s, 2H); 3.18 (d, J=6.5 Hz, 2H); 2.24 (s, 2H); 2.13 (d, J=6.5 Hz, 2H); 1.6-2.1 (m, 1H); 0.9 (d, J=6.5 Hz, 6H).
42	trans	δ = 8.2-8.35 (m, 1H); 7.65-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.26 (d, J=16 Hz, 1H); 5.86 (dt, J=16 + 2 x 6.5 Hz, 1H); 4.95 (s, $=C\langle^{H}_{H}$); 3.90 (s, 2H); 3.18 (d, J=6.5 Hz, 2H); 2.24 (s, 3H); 2.15-2.35 (m, 2H); 1.1-1.7 (m, 4H); 0.9 (ps.t, 3H).
43	trans	δ = 8.2-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.30 (d, J=15.5 Hz, 1H); 6.02 (dt, J=15.5 Hz + 2 x 6.5 Hz, 1H); [5.07 (sbr, 1H) + 4.80 (d, J=2 Hz, 1H), $=C\langle^{H}_{H}$]; 3.9 (s, 2H); 3.16 (d, 2H); 2.25 (s, 3H); 1.1 (s, 9H).
6,45	trans	δ = 8.2-8.35 (1 arom. H); 7.7-7.9 (2 arom. H); 7.3-7.6 (4 arom. H); 6.52 (dd, 1 olef. H, J=15 u. 10 Hz); 5.86 (d, 1 olef. H, J=10 Hz); 5.79 (dt, 1 olef, H, J= 15 + 2 x 6.5 Hz); 3.92 (s, 2H); 3.20 (d, J= 6.5 Hz, 2H); 2.25 (s, 3H); 2.1-2.4 (m, 4H); 1.6 (br, 6H)

Example	Isomer	Spectrum
46	trans	δ= 8.15-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.3 (dt, J=16 + 2x6.5 Hz, 1H); 5.7 (dm, J=16 Hz, 1H); 4.34 (d, J=2 Hz, 2H); 3.9 (s, 2H); 3.16 (d, J=6.5 Hz, 2H); 2.24 (s, 3H); 2.2 (CH).
47	trans	δ= 8.2-8.35 (m, 1H); 7.65-7.9 (m, 2H); 7.3-7.5 (m, 4H); 6.17 (dd, J=16 + 7 Hz, 1H); 5.58 (dm, J= 16 Hz, 1H); 3.9 (AB-System, 2H); 3.25 (m, 1H); 2.1-2.3 (m, 2H); 2.14 (s, 3H); 1.3-1.6 (m, 4H); 1.18 (d, J=7 Hz, 3H); 0.85 (m, 3H).
48	cis	δ= 8.2-8.35 (m, 1H); 7.6-7.9 (m, 2H); 7.3-7.6 (m, 4H); 5.98 (dd, J=11 + 9 Hz, 1H); 5.6 (dm, J=11 Hz, 1H); 3.96 (AB-System, 2H); 3.8 (m, 1H); 2.1-2.3 (m, 2H); 2.16 (s, 3H); 1.2-1.6 (m, 4H); 1.26 (d, J=7 Hz, 3H); 0,82 (m, 3H).
49	trans	δ= 8.15-8.35 (m, 1H); 7.6-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.14 (dt, J=16 + 2x6.5 Hz, 1H); 5.66 (dm, J=16 Hz, 1H); 3.86 (s, 2H); 3.10 (d, J=6.5 Hz, 2H); 2.2 (s, 3H); 1.4 (qua, J=7 Hz, 2H); 1.15 (s, 6H); 0.9 (t,J=7 Hz, 3H).
50	cis	δ= 8.2-8.35 (m, 1H); 7.6-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.0 (dt, J=11 + 2x6.5 Hz, 1H); 5.64 (dm, J=11 Hz, 1H); 3.9 (s, 2H); 3.35 (d, J=6.5 Hz, 2H); 2.22 (s, 3H); 1.45 (qua, J=7 Hz, 2H); 1.18 (s, 6H); 0.95 (t, J=7 Hz, 3H).
51	trans	δ= 8.15-8.35 (m, 1H); 7.6-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.16 (dt, J=16 + 2x6.5 Hz, 1H); 5.66 (dm, J=16 Hz, 1H) 3.86 (s, 2H); 3.10 (d, J=6.5 Hz, 2H); 2.7 (br, 1H);

Example	Isomer	Spectrum
52	cis	δ = 8.15-8.35 (m, 1H); 7.6-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6.0 (dt, J=11 + 2x6.5 Hz, 1H); 5.64 (dm, J=11 Hz, 1H); 3.9 (s, 2H); 3.36 (d, J=6.5 Hz, 2H); 2.75 (br, 1H); 2.22 (s, 3H); 1.4-2.1 (m, 8H).
55	trans	δ = 7.8-8.1 (m, 2H); 7.25-7.5 (m, 3H); 6.50 (dd, J=17 + 12 Hz, 1H); 5.85 (d, J=12 Hz, 1H); 5.74 (dt, J=17 u. 2x7 Hz, 1H); 3.77 (s, 2H); 3.14 (d, J=7 Hz, 2H); 2.0-2.4 (m, 4H); 2.25 (s, 3H); 1.55 (sbr, 6H).
56	trans	δ = 8.2-8.4 (m, 2H); 7.25-7.7 (m, 3H); 6.74 (d, J=8 Hz, 1H); 6.2 (dt, J=18 + 2x7 Hz, 1H); 5.67 (dt, J=18 u. 2x15 Hz, 1H); 4.0 (s, 3H); 3.82 (s, 2H); 3.10 (dd, J=7 u. 1.5 Hz); 2.2 (s, 3H); 1.24 (s, 9H).
57	cis	δ= 8.2-8.4 (m, 2H); 7.25-7.7 (m, 3H); 6.74 (d, J=8 Hz, 1H); 5.05 (dt, J=12 + 2x7.5 Hz, 1H); 5.65 (dt, J=12 u. 2x1.5 Hz, 1H); 4.0 (s, 3H); 3.85 (s, 2H); 3.35 (dd, J=7.5 u. 1.5 Hz, 2H); 2.24 (s, 3H); 1.26 (s, 9H).
58	trans	δ= 7.2-7.8 (m, 6H); 6.44 (dd, J=17 + 12 Hz, 1H); 5.80 (d, J=12 Hz, 1H); 5.66 (dt, J=17 + 2x7 Hz, 1H); 5.0 (t, J=6 Hz, 1H); 3.33 (d, J=6 Hz, 2H); 3.14 (d, J=7 Hz, 2H); 2.0-2.4 (m, 4H); 2.12 (s, 3H); 1.5 (sbr, 6H).
59	trans	δ= 7.1-7.7 (m,6H); 6.04 (dt,J=16 + 2x6.5 Hz, 1H); 5.6 (dm,J=16 Hz, 1H); 4.9 (t,J=6 Hz, 1H); 3.22 (d,J=6 Hz, 2H); 3.0 (d,J=6.5 Hz, 2H); 2.1 (s, 3H); 1.18 (s, 9H).

Example	Isomer	Spectrum
53	trans	δ= 8.15-8.35 (m, 1H); 7.6-7.9 (m, 2H); 7.3-7.6 (m, 4H); 6,15 (dt,J=16 + 2x6.5 Hz, 1H); 5.65 (dm, J=16 Hz, 1H); 3.85 (s, 2H); 3.10 (d, J= 6.5 Hz, 2H); 2.2 (s, 3H); 1.8-2.1 (br, 9H); 1.6-1.8 (br, 6H).

The required starting materials can be obtained e.g. as follows.

1. Compounds of formula IV:

A) (3-Benzo[b]thiophenemethyl)methylamine (for Ex. 1)

3-Chloromethylbenzo[b]thiophene is dissolved in benzene, added dropwise to a ca. 10-fold excess of methylamine in ethanol at 0-5° and then stirred for 16 hours at room temperature. The crude mixture is concentrated under vacuum, the residue partitioned between methylenechloride and 1N NaOH and the organic phase dried and evaporated under vacuum. The purified product is obtained by vacuum distillation b.p. 90-94°/1,33 Pa.

B) (3-Benzo[b]furanmethyl)methylamine (for Ex. 12 and 13)

Obtained analogously to Example A) b.p. 105-110°/5.3 Pa.

C) 2-(1-Naphthyl)piperidine (for Ex. 15, 34 and 35)

A Grignard complex is prepared by adding 43.4g of 1-bromonaphthaline in absolute ether dropwise to 5.1g of magnesium in 50 ml of absolute ether. The ether is removed from the reaction mixture and replaced by absolute benzene. 8g 6-Methoxy-2,3,4,5-tetrahydropyridine are added to the boiling reaction mixture. After a further 8 hours the mixture is cooled, treated with saturated aqueous ammoniumchloride solution and the reaction product removed from the organic phase by shaking with aqueous HCl-solution.

After neutralisation and working up the 2-(1-naphthyl)-3,4,5,6-tetrahydropyridine is dissolved directly in methanol and reduced with $NaBH_4$. After normal working up the product is converted with alcoholic HCl solution to its hydrochloride. M.p. 287-289° (after intensive drying under high vacuum 328-329°).

2. Compounds of formula V:

D) 1-Bromo-6,6-dimethyl-2-hepten-4-yne (for Ex. 16, 17, 56, 57 and 59)

a) 6,6-Dimethyl-1-hepten-4-yn-3-ole

38 ml 3,3-Dimethyl-1-butyne are dissolved in abs. tetrahydrofuran and 172 ml of a 20% solution of n-butyl-lithium added dropwise under protective gas at a temperature of -20°. The reaction mixture is then cooled to -75° and 19.3 g acrolein in 20 ml of tetrahydrofuran added dropwise. The mixture is warmed to room temperature, reacted with saturated aqueous NH_4Cl and extracted a number of times with ether. The organic phase is dried, concentrated and the purified product obtained by vacuum distillation, b.p. 70-72°/1600 Pa.

b) 1-Bromo-6,6-dimethyl-2-hepten-4-yne

50 ml 48% HBr and 10g PBr_3 are stirred at 40° until a homogenous mixture is obtained. An alcoholic solution of 13.5g 6,6-dimethyl-1-hepten-4-yn-3-ole are added

dropwise at 10° and stirred for $1^1/2$ hours at room temperature. The reaction mixture is poured onto ice and extracted a number of times with hexane. The organic phase is washed a number of times with aqueous NaCl, dried and concentrated. NMR-spectography shows that the oily product comprises a 3:1 mixture of trans- and cis-1-bromo-6,6-dimethyl-2-hepten-4-yne and is taken directly for alkylation.

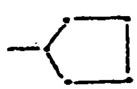
NMR: δ = 5.5 - 6.4 (m, 2 olef. H), [4.15 (d. J = 8Hz) and 3.95 (d, J = 8Hz) in ratio 1:3, 2H, = CH-$\underline{CH_2}$Br], 1.20 (m, 9H).

Analogously to D) above the following compounds of formula V can be obtained.

Table II

a) $R_5-CH=CH-\underset{}{\overset{OH}{\overset{|}{C}}}H-C\equiv C-R_{11}$

b) $A-\underset{R_5}{\underset{|}{C}}H-CH=CH-C\equiv C-R_{11}$

	R_{11}	R_5	A	Physical data	for Ex.
E) a b	$-CH\begin{matrix}CH_3\\C_2H_5\end{matrix}$	H	– Br	b.p. 75-80°/1460 Pa oil	20,21
F) a b	$-CH_2.CH\begin{matrix}CH_3\\CH_3\end{matrix}$	H	– Br	b.p. 87-91°/1730 Pa oil	22,23
G) a b	$-\overset{CH_3}{\underset{CH_3}{C}}-C_2H_5$	H	– Br	b.p. 90°/1460 Pa oil	49,50
H) a b		H	– Br	b.p. 94-96°/800 Pa oil	51,52
I) a b	$-(CH_2)_3-CH_3$	CH_3	– Br	b.p. 92-93°/530 Pa oil	47,48

The remaining compounds of formula V can be obtained analogously to D) above.

3. Compounds of formula VIII

M) N-Methyl-N-(1-naphthylmethyl)octa-2,4-diynyl-1-amine (for Ex. 31)

9g 1,3-Heptadiyne, 16g methyl-(1-naphthylmethyl)-amine, 2.8g paraformaldehyde and 1.3g $ZnCl_2$ (anhydrous) are heated for 3 hours at 100° in absolute dioxane. After cooling the solvent is removed under vacuum, the residue partitioned between chloroform and aqueous $NaHCO_3$-solution and the organic phase dried and concentrated. The purified product is obtained by chromatography over kieselgel (toluene/ethyl acetate 9:1) as an oil.

N) N-Methyl-N-(1-naphthylmethyl)-2,4-nonadiynyl-1-amine (for Ex. 3)

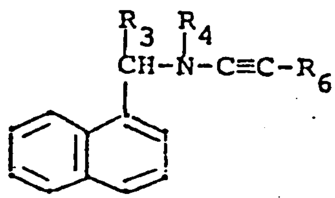
8.25g 1-Bromohexyne are added dropwise to a mixture of 16g N-methyl-N-(1-naphthylmethyl)-propargylamine, 0.5g $NH_2OH.HCl$, 0.25g CuCl and 20 ml 70% ethylamine. The reaction mixture is stirred overnight at room temperature, treated with an aqueous solution of 1g KCN and extracted a number of times with ether. The organic phase is washed with saturated aqueous NaCl, dried and evaporated. The title substance is obtained as an oil after chromatography over Kieselgel (eluant toluene/ethyl acetate 95:5).

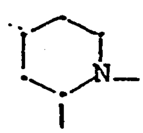
O) N-Methyl-N-(1-naphthylmethyl)-4-t.butyl-pent-2-yn-4-enyl-1-amine (for Ex. 43)

933 mg N-Methyl-N-(1-naphthylmethyl)-4-hydroxy-4,5,5-trimethyl-2-hexynyl-1-amine are dissolved in abs. pyridine, warmed to 50° and 0.4 ml $POCl_3$ added. Stirring is carried out for one hour at 90°, the mixture poured onto ice and the reaction product isolated as an oil by extraction with ether and chromatography over kieselgel (eluant toluene/ethyl acetate 9:1).

Analogously to M), N) and O) above, the following compounds of formula VIII may be obtained.

Table III



	R_3	R_4	R_6	Physical data	For Ex.
P)	H	CH_3	$-C\equiv C-(CH_2)_4-CH_3$	oil	32
Q)	H	CH_3	$-C\equiv C-(CH_2)_5-CH_3$	oil	33
R)	H	CH_3	$-C\equiv C-C(CH_3)_3$	oil	16
S)	$R_3 + R_4 + N$		$-C\equiv C-(CH_2)_2-CH_3$	oil	34
T)			$-C\equiv C-(CH_2)_3-CH_3$	oil	35

The remaining compounds of formula VIII can be prepared analogously to M), N) and O) above.

4. Compounds of formula If

U) N-Methyl-N-(1-naphthylmethyl)-4-hydroxy-4-cyclohexyl-2-pentenyl-1-amine (for Ex. 5)

a) N-Methyl-N-(1-naphthylmethyl)-4-hydroxy-4-cyclohexyl-pent-2-ynyl-1-amine

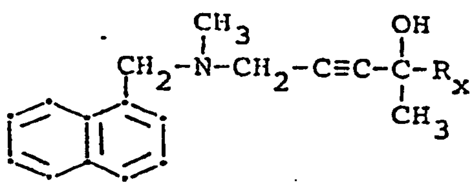
10.7 ml of a 15% solution of BuLi in hexane are added dropwise to 3g N-methyl-N-(1-naphthylmethyl)propargyl amine in absolute tetrahydrofuran and after 30 minutes reacted with a solution of 1.79g cyclohexyl-methyl ketone. Stirring is continued for 24 hours at room temperature and the mixture poured onto ice and extracted with ether. The organic phase is washed, dried and concentrated under vacuum. Chromatography over kieselgel (eluant toluene/ethylacetate 4:1) yields the title product as an oil.

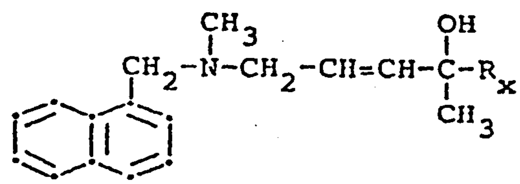
b) N-Methyl-N-(1-naphthylmethyl)-4-hydroxy-4-cyclohexyl-2-pentenyl-1-amine

10g of the substance obtained under a) are dissolved in tetrahydrofuran and added dropwise to a suspension of 1.4g $LiAlH_4$ in abs. tetrahydrofuran and the mixture refluxed for 3 hours. Excess reagent is destroyed with ethyl acetate/H_2O. After extraction with ether, drying and evaporation under vacuum followed by chromatography over kieselgel (eluant $CHCl_3/C_2H_5OH$ 95:5) the title product is obtained as an oil.

Analogously to U) above the following compounds can be obtained.

Table IV

a) 

b) 

	R_x	physical data [a) and b)]	For Ex.
V) a) b)	$-CH_2-CH(CH_3)_2$	oil	41
W) a) b)	$-(CH_2)_3-CH_3$	oil	42
X) a) b)	$-C(CH_3)_3$	oil	43
Y) a) b)	$-C_6H_5$	oil	40

Compounds of formula IX can be prepared analogously to Example 6 above and are preferably taken directly without further purification or isolation for the final step.

Example		Spectrum
N)		δ = 8.2-8.35 (1 arom. H); 7.7-7.9 (2 arom. H); 7.3-7.6 (4 arom. H); 3.97 (s, 2H); 3.37 (s, 2H); 2.40 (s, 3H); 2.2.-2.4 (m, 2H); 1.2-1.8 (4H); 0.8-1.05 (m, 3H).
M)		identical with N) except: δ = 2.28 (t, 2H); 1.58 (sext., 2H); 1.0 (t, 3H).
P)		identical with N) except: δ = 1.2-1.8 (m, 6H).
Q)		identical with N) except: δ = 1.2-1.8 (m, 8H).
R)		δ = 8.1-8.25 (m, 1H); 7.6-7.85 (m, 2H); 7.2-7.5 (m, 4H); 3.92 (s, 2H); 3.33 (s, 2H); 2.35 (s,3H); 1.22 (s, 9H).
S)		δ = 8.5 (br, 1H); 7.3-7.9 (m, 6H); 4.05 (br, 1H); 3.24 (s, 2H); 3.12 (m, 1H); 2.5-2.8 (m, 1H); 2.26 (t, J=6.5 Hz, 2H); 1.6-2.0 (m, 6H); 1.56 (sext., J=7 Hz, 2H); 0.99 (t, J=7 Hz, 3H).
T)		identical with S) except: δ = 2.28 (ps.t, 2H); 1.3-1.7 (m, 4H); 0.91 (ps.t, 3H).

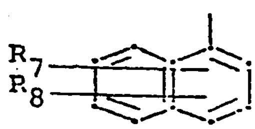
Example		Spectrum
U)	a)	δ = 8.2-8.35 (1 arom. H); 7.7-7.9 (2 arom. H); 7.3-7.6 (4 arom. H); 4.0 (s, 2H); 3.37 (s, 2H); 2.38 (s, 3H); 1.52 (s, 3H); 1.0-2.2 (11H).
	b)	δ = 8.2-8.35 (1 arom. H); 7.7-7.9 (2 arom.H); 7.3-7.6 (4 arom. H); 5.76 (m, 2 olef. H); 3.91 (s, 2H); 3.13 (m, 2H); 2.25 (s, 3H); 1.23 (s, 3H); 0.8-2.0 (11H).
V)	a)	δ = 8.15-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 3.95 (s, 2H); 3,34 (s, 2H); 2.35 (s, 3H); 1.8-2.3 (m, 1H); 2.0 (s, O<u>H</u>); 1.62 (d, J=6.5 Hz, 2H); 1.53 (s, 3H); 1.04 u. 1.02 (2 d, J= 6.5 Hz, Σ 6H).
	b)	δ = 8.2-8.4 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 5.78 (AB-portion of an ABX_2-system, 2 olef. H); 3.90 (s, 2H); 3.12 (m, 2H); 2.22 (s, 3H); 1.3-2.0 (m, 1H); 1.5 (s, O<u>H</u>); 1.4 (d, 2H); 1.3 (s, 3H); 0.92 u. 0.90 (2 d, J=7 Hz., Σ 6H).
W)	a)	δ = 8.2-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 3.98 (s, 2H); 3.36 (s, 2H); 2.38 (s, 3H); 2.1 (br, O<u>H</u>); 1.2-1.9 (m, 6H); 1.56 (s, 3H); 0.95 (ps.t., 3H).
	b)	δ = 8.2-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 5.85 (AB-portion of an ABX_2-system, 2H); 3.90 (s, 2H); 3.12 (m, 2H); 2.25 (s, 3H); 1.2-1.7 (m, 6H + O<u>H</u>); 1.28 (s, 3H); 0.9 (ps.t., 3H).

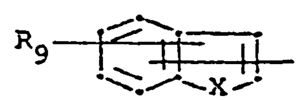
Example		Spectrum
X)	a)	δ = 8.2-8.35 (m, 1H); 7.7-7.9 (m, 2H); 7.3-7.6 (m, 4H); 4.0 (s, 2H); 3.38 (s, 2H); 2.4 (s, 3H); 1.96 (br, OH); 1.54 (s, 3H); 1.14 (s, 9H).
	b)	δ = 8.2-8.4 (m, 1H); 7.65-7.9 (m, 2H); 7.3-7.6 (m, 4H); 5.6-6.1 (AB-portion of an ABX_2-system, J=15 + 2x5.5 Hz, 2H); 3.92 (s, 2H); 3.16 (d, 2H; J=5.5 Hz); 2.25 (s, 3H); 1.4 (br, OH); 1.26 (s, 3H); 0.96 (s, 9H).
Y)	a)	δ = 8.2-8.35 (m, 1H); 7.6-7.9 (m, 4H); 7.2-7.6 (m, 7H); 4.0 (s, 2H); 3.4 (s, 2H); 2.65 (br,OH); 2.4 (s, 3H); 1.85 (s, 3H).
	b)	8.15-8.35 (m, 1H); 7.65-7.9 (m, 2H); 7.2-7.6 (m, 9H); 5.6-6.1 (AB-portion of an ABX_2-system, J=15 Hz + 2x5.5 Hz, 2H); 3.88 (s, 2H); 3.13 (d, J=5.5 Hz, 2H); 2.24 (s, 3H); 2.0 (s, OH); 1.65 (s, 3H).

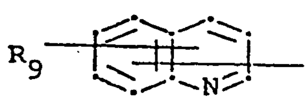
1. A compound of formula I,

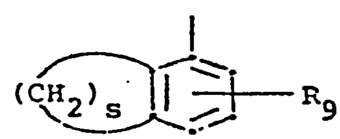
$$R_2 - \underset{\substack{| \\ R_3}}{\overset{\substack{R_1 \\ |}}{C}} - \overset{\substack{R_4 \\ |}}{N} - \overset{\substack{R_5 \\ |}}{CH} - CH = CH - R_6 \qquad \text{I}$$

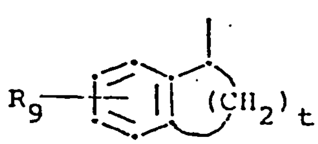
wherein a) R_1 represents a group of formula

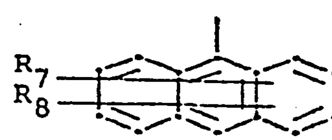

IIa


IIb

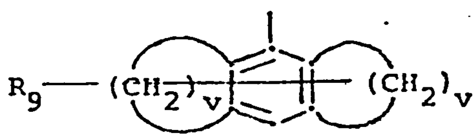

IIc


IId


IIe

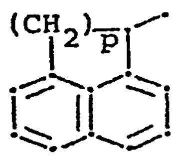

IIf

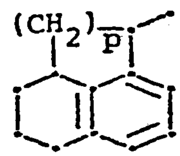
or

 IIg

and R_2 represents hydrogen or lower alkyl,

or R_1 and R_2 together represent a group of formula

 IIh

 IIi

whereby in the formulae IIa to IIi,

R_7 and R_8 represent, independently, hydrogen, halogen, trifluoromethyl, hydroxy, nitro, lower alkyl or lower alkoxy,

R_9 represents hydrogen, halogen, hydroxy, lower alkyl or lower alkoxy,

X represents oxygen, sulphur, imino, lower alkyl imino or a radical of formula $-(CH_2)_r-$,

p is 1, 2 or 3,

r is 1, 2 or 3,

s is 3, 4 or 5,

t is 2, 3 or 4, and

v is 3, 4, 5 or 6;

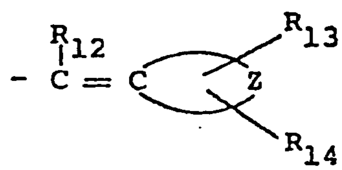
R_3 and R_5 represent, independently, hydrogen or lower alkyl and

R_4 represents C_{1-6}alkyl or C_{3-8} cycloalkyl-(C_{1-6})-alkyl; and

R_6 represents a group of formula

$-C \equiv C - R_{11}$ IIIa $\qquad$ $-\underset{\displaystyle R_{11}}{\underset{|}{C}} = CH_2$ IIIb

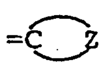
oder



IIIc

wherein R_{11} represents hydrogen, optionally α-hydroxy substituted alkyl; alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, phenyl, phenalkyl or thienyl,

R_{12}, R_{13} and R_{14} represent, independently, hydrogen or lower alkyl, and

 represents a C_{5-8} cycloalkylidene radical optionally containing a double bond; or

b) R_1 represents a group of formula IIa to IIg as defined under a),

R_2 represents hydrogen or lower alkyl,

R_3 and R_4 together form a group $-(CH_2)_u-$, wherein u is an integer of 1 to 8, and

R_5 and R_6 have the meanings given under a).

2. A compound as claimed in Claim 1 wherein

a) R_1 represents a group of the formula IIa, IIb, IIe,
R_2 represents hydrogen,
R_3 represents hydrogen,
R_4 represents lower alkyl,
R_5 represents hydrogen or lower alkyl,
or R_3 and R_4 together form a group $-(CH_2)_u-$ or

b) wherein R_1 and R_2 together represent a group of the formula IIh,
R_3 represents hydrogen,
R_4 represents lower alkyl,
R_5 represents lower alkyl and
R_6 is as defined in Claim 1.

3. A compound as claimed in Claim 1 or Claim 2 wherein R_6 represents a group of formula IIIa as defined in Claim 1.

4. A compound as claimed in any one of Claims 1 to 3 wherein R_1 represents a group of formula IIa as defined in Claim 1.

5. A compound as claimed in any one of Claims 1 to 4 wherein the double bond between the group R_6 and the nitrogen atom is in the trans configuration.

6. A compound as claimed in any one of Claims 1 to 5 wherein R_{11} represents alkyl, alkenyl, alkynyl, cycloalkylalkyl, phenyl or phenalkyl and all other substituents are as defined in Claim 1.

7. N-Methyl-N-(1-naphthylmethyl)-non-2(trans)-en-4-ynyl-1-amine.

8. N-Methyl-N-(1-naphthylmethyl)-6,6-dimethyl-hept-2(trans)-en-4-ynyl-1-amine.

9. A compound as claimed in any one of Claims 1 to 8 in free base form.

10. A compound as claimed in any one of Claims 1 to 8 in the form of an acid addition salt thereof.

11. A compound as claimed in Claim 10 in the form of its hydrochloride.

12. A compound as claimed in any one of Claims 1 to 11 substantially as hereinbefore described with reference to Examples 1 to 6 and Table I.

13. A chemotherapeutical composition comprising a compound as claimed in any one of Claims 1 to 8 or 12 or a chemotherapeutically acceptable acid addition salt thereof in admixture with a chemotherapeutically acceptable diluent or carrier.

14. A compound as claimed in any one of Claims 1 to 11 for use as a chemotherapeutic agent.

15. A compound as claimed in any one of Claims 1 to 12 for use as an antimycotic agent.

16. A compound as claimed in any one of Claims 1 to 12 for use in the treatment of the human or animal body by therapy.

17. A method of treating diseases or infections caused by mycetes in man or other animals which comprises administering to a subject in need of treatment an effective amount of a compound as claimed in any one of Claims 1 to 8 or 12 or a chemotherapeutically acceptable acid addition salt thereof.

18. A process for the production of compounds of formula I as defined in Claim 1 which comprises

a) when R_6 represents a group of formula IIIa, as defined above, (compound Ia), reacting a compound of formula IV,

$$\begin{array}{c} R_1 \\ | \\ R_2 - C - NH - R_4 \\ | \\ R_3 \end{array} \qquad IV$$

wherein R_1 to R_4 are as defined above, with a compound of formula V,

$$\begin{array}{l} \quad\;\; R_5 \\ \quad\;\; | \\ A - CH - CH = CH - R_6' \end{array} \qquad V$$

wherein A is a leaving group, R_5 is as defined above and R_6' stands for a group of formula IIIa, as defined above, or

b) when R_6 represents a group of formula IIIa, wherein R_1 represents α-hydroxyalkyl (compounds Ib), reacting a meta ated compound of formula Ic,

$$R_2 - \overset{\displaystyle R_1}{\underset{\displaystyle R_3}{\overset{|}{\underset{|}{C}}}} - \overset{\displaystyle R_4}{\overset{|}{N}} - \overset{\displaystyle R_5}{\overset{|}{CH}} - CH = CH - C \equiv CH \qquad Ic$$

wherein R_1 to R_5 are as defined above, with a carbonyl compound of formula VII,

$$R_{15}.CO.CH\begin{matrix}\nearrow R_{16}\\ \searrow R_{17}\end{matrix} \qquad \text{VII}$$

wherein R_{15}, R_{16} and R_{17} represent independently hydrogen or lower alkyl, or

c) when the double bond between R_6 and the nitrogen atom is in trans configuration (compounds Id) reducing a compound of formula VIII,

$$R_2 - \underset{\displaystyle R_3}{\overset{\displaystyle R_1}{C}} - \overset{\displaystyle R_4}{N} - \overset{\displaystyle R_5}{CH} - C \equiv C - R_6 \qquad \text{VIII}$$

wherein R_1 to R_6 are as defined above, with diisobutylaluminiumhydride, or

d) when R_6 represents a group of IIIb or IIIc as defined above or a group of formula IIId,

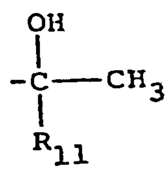
$$-C \equiv C - \underset{\displaystyle R_{15}}{C} = C\begin{matrix}\nearrow R_{16}\\ \searrow R_{17}\end{matrix} \qquad \text{IIId}$$

wherein R_{15}, R_{16} and R_{17} are as defined above (compounds Ie) splitting off water from a compound of formula

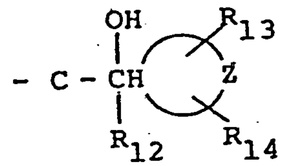
$$R_2 - \underset{\displaystyle R_3}{\overset{\displaystyle R_1}{C}} - \overset{\displaystyle R_4}{N} - \overset{\displaystyle R_5}{CH} - CH = CH - R_6''' \qquad \text{If}$$

wherein R_1 to R_5 are as defined above,

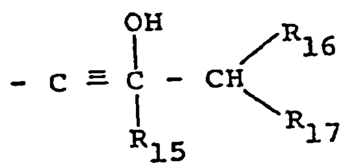
and R_6''' represents a group of formula IIIe, IIIf, or IIIg,



IIIe ;



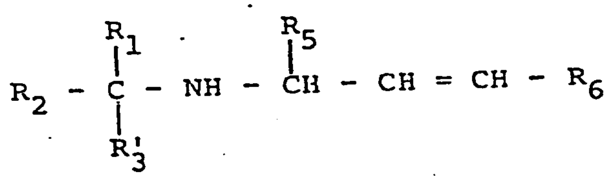
IIIf



IIIg

wherein R_{11} to R_{17} and Z are as defined above, or

e) when R_3 represents hydrogen or lower alkyl and R_4 represents C_{1-6}alkyl or C_{3-8}cycloalkyl-(C_{1-6})-alkyl (compounds Ig), introducing the group R_4' into a compound of formula IX,



IX

wherein R_1, R_2, R_5 and R_6 are as defined above,

R_3' represents hydrogen or lower alkyl, and

R_4' represents C_{1-6}alkyl or C_{3-8}cycloalkyl-(C_{1-6})-alkyl.

19. A process as claimed in Claim 18 substantially as hereinbefore described with reference to the Examples.

20. All steps, features, compositions and compounds of the invention referred to or indicated in the specification and/or claims of this application, individually or collectively and any and all combinations or any two or more of said steps or features.

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European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

Application number

EP 80 10 4623

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.³)
	EP - A - 0 000 896 (SANDOZ) * Claims * --	1,13-16, 18,19	C 07 C 87/28 87/45 93/14 C 07 D 211/14 307/81 333/58 A 61 K 31/13 31/34 31/38 31/445
	FR - A - 2 349 566 (SANDOZ) * Claims * ----	1,13-16, 18-19	

TECHNICAL FIELDS SEARCHED (Int.Cl.³)

C 07 C 87/28
87/45
93/14
C 07 D 211/14
307/81
333/58

INCOMPLETE SEARCH

The Search Division considers that the present European patent application does not comply with the provisions of the European Patent Convention to such an extent that it is not possible to carry out a meaningful search into the state of the art on the basis of some of the claims.

Claims searched completely: 1-11,13-16, 18-19

Claims searched incompletely:

Claims not searched: 17(art.52(4); 12,20 (art.29(6)

Reason for the limitation of the search:

Method for treatment of the human or animal body by surgery of therapy (See Art, 52(4) of the European Patent Convention)

Art. 29(6) of the European Patent convention, concerning form and content of claims.

CATEGORY OF CITED DOCUMENTS

X: particularly relevant
A: technological background
O: non-written disclosure
P: intermediate document
T: theory or principle underlying the invention
E: conflicting application
D: document cited in the application
L: citation for other reasons

&: member of the same patent family, corresponding document

Place of search	Date of completion of the search	Examiner
The Hague	18-11-1980	MOREAU

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